REMARKS

Entry of the foregoing, reexamination and reconsideration of the above-identified application, pursuant to and consistent with 37 C.F.R. § 1.116, are respectfully requested.

Status

Prior to the instant Amendment and Reply After Final Rejection Pursuant To 37 C.F.R. § 1.116, Claims 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, 38, and 42-44 were pending. *See Final Official Action Mailed*[1] *February 5, 2007, Office Action Summary, Item 4.* Claims 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, 38, and 44 stand rejected. *Id. at Item 6.* Claims 42 and 43 were withdrawn from consideration as purportedly being directed to a non-elected invention. *See Official Action mailed April 14, 2004, Page 2, ¶¶ 1-4.*

Telephonic Interview

Applicants and Applicants' undersigned representative wish to thank Examiner Zeman for the courtesies extended during a telephonic interview ("the Interview") conducted among Examiner Zeman, Applicants, and Applicants' undersigned representative (Erin M. Dunston, Registration No. 51, 147) on May 1, 2007. As is correctly reflected in the Interview Summary provided by Examiner Zeman by facsimile on May 14, 2007 (yet which has not yet posted in PAIR as of the filing date of this Amendment And Reply After Final Rejection), the pending claims and the cited publications were discussed. During the Interview, Applicants discussed the nature of their claimed invention and explained to Examiner Zeman why the cited publications neither disclose nor suggest Applicants'

[1] While the Final Official Action lists a mailing date of February 5, 2007, the Final Office Action was returned to the Patent and Trademark Office on February 12, 2007 as "undelivered." On April 19, 2007, Applicants filed a Petition To The Director Pursuant To 37 C.F.R. § 1.181(a) To Reset The Period For Reply Due To Late Receipt Of An Office Action. At the time of filing this Amendment and Reply After Final Rejection, Applicants have not yet learned whether their Petition was granted.

invention. Further during the Interview, Examiner Zeman expressed her appreciation that the cited publications teach away from Applicants' invention and indicated her willingness to entertain an Amendment and Reply After Final Rejection.

Summary of Claim Amendments

By the foregoing claim amendments, Applicants have made a number of amendments to further clarify Applicants' invention:

Claim 1 has been amended to specify that the sequencing *performed on* the deoxyribonucleic acid from each bacterium sample is *DNA* sequencing. Claim 1 has also been amended to specify that it is *nucleotide* sequence data that is stored in the database and compared. Support for these amendments may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines 15-16 and 21-23; Page 11, Lines 9-19; and Figures 1, 4A, and 4B. Accordingly, no new matter has been added.

Claim 3 has been amended to specify that the centralized database is located *at a different location* from where the sample is obtained. Support for this amendment may be found throughout the Specification, and at least at Page 8, Lines 3-12; Page 10, Lines 15-16; Page 11, Lines 5-6; Page 11, Line 20 to Page 13, Line 22; Figures 1, 7A and 7B. Accordingly, no new matter has been added.

Claim 7 has been amended to depend from independent Claim 1, as opposed to dependent Claim 6. Support for this amendment may be found throughout the Specification, and at least at Page 8, Lines 17-21 and at original Claims 1, 6, and 7. Accordingly, no new matter has been added.

Claim 8 has been amended to depend from independent Claim 1, as opposed to dependent Claim 7. Support for this amendment may be found throughout the Specification, and at least at Page 18, Lines 1-3; Page 27, Lines 9-14; and at original Claims 1, 7, and 8. Accordingly, no new matter has been added.

Claim 10 has been amended to change "including" to "comprising" so as to mirror the format of the majority of the other claims. This amendment is clerical in nature and no new matter has been added.

Claim 11 has been amended to specify that *the information contained within the patient's medical history is segregated into private information and non-private information* and that *it is the non-private information that is transmitted to the database*, whereas *the patient's private information is not transmitted.* Further, the patient's private information is stored in a database *whose location is different* from the database to which the patient's non-private information is transmitted. Support for these amendments may be found throughout the Specification, and at least at Page 16, Lines 9-15. Accordingly, no new matter has been added.

Claim 12 has been amended to specify that the *DNA* sequencing *performed* comprises either sequencing the first region at a *physically separate* facility and transmitting the resulting *nucleotide* sequence data to the database via a computer network, or sending the bacterium samples themselves to an infection control facility *that has access to* the database, sequencing the first region at that infection control facility, and storing the *nucleotide* sequence data in the database. Support for these amendments may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines 15-16 and 21-23; Page 11, Lines 9-19; and Figures 1, 4A, and 4B. Accordingly, no new matter has been added.

Claim 14 has been amended to specify that it is *DNA* sequencing that is performed. Support for this amendment may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines 15-16 and 21-23; Page 11, Lines 9-19; and Figures 1, 4A, and 4B. Accordingly, no new matter has been added.

Claim 16 has been amended to specify that the phylogenetic relatedness between *at least two* compared samples comprises identifying repeat sequences in the *nucleotide*

sequence data *from each sample* and treating the insertion or deletion of a repeat sequence as a single genetic event. Support for this amendment may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines 15-16 and 21-23; Page 11, Lines 9-19; Page 24, Lines 19-21; Page 28, Line 15 to Page 36, Line 18; and Figures 1, 3, 4A, 4B, 5, and 6. Accordingly, no new matter has been added.

Claim 17 has been amended to depend from independent Claim 1 and to specify that the phylogenetic relatedness between *at least two* compared samples comprises *identifying individual single nucleotide polymorphisms in the nucleotide sequence data from each sample* and treating the insertion or deletion *or change* of an individual nucleotide as a single genetic event. Support for this amendment may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines 15-16 and 21-23; Page 11, Lines 9-19; Page 24, Lines 19-21; Page 28, Line 15 to Page 36, Line 18; Figures 1, 3, 4A, 4B, 5, and 6; and original Claims 1, 16, and 17. Accordingly, no new matter has been added.

Claim 21 has been amended to specify that the phylogenetic relatedness between *at least two* compared samples of *nucleotide sequence data* includes at least one of determining local, regional, and global relatedness, where, with regard to local relatedness, the at least two samples are obtained from the same *location.* Support for these amendments may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines 15-16 and 21-23; Page 11, Lines 9-19; Page 23, Lines 4-11; Page 25, Line 6; and Figures 1, 4A, and 4B. Accordingly, no new matter has been added.

Claim 22 has been amended to specify that the *nucleotide sequence data* is transmitted over a computer network. Support for this amendment may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines 15-16 and 21-23; Page 11, Lines 9-19; and Figures 1, 4A, and 4B. Accordingly, no new matter has been added.

Claim 23 has been amended to correct a typographical and/or linguistic issue. Accordingly, no new matter has been added.

Claim 24 has been amended to specify that the patient's physical location is *determined with a sensor*. Support for this amendment may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines 15-16 and 21-23; Page 11, Lines 9-19; Page 26, Lines 1-13; and Figures 1, 4A, and 4B. Accordingly, no new matter has been added.

Claim 25 has been amended to change "including" to "comprising" so as to mirror the format of the majority of the other claims. This amendment is clerical in nature and no new matter has been added.

Claim 27 also has been amended to change "including" to "comprising" so as to mirror the format of the majority of the other claims. This amendment is clerical in nature and no new matter has been added.

Claim 28 has been amended to specify that it is *DNA* sequencing that is *performed* on a second region of *deoxyribonucleic* acid of each bacterium sample, that the *nucleotide* sequence data is stored, that the *nucleotide sequence data* from the second sequence region of at least two of the plurality of samples is compared *to nucleotide sequence data already stored in the database*, and that the phylogenetic relatedness is determined. Support for these amendments may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines 6-9, 15-16, and 21-23; Page 11, Lines 9-19; Page 23, Lines 12-15; Page 34, Lines 3-7; and Figures 1, 4A, and 4B. Accordingly, no new matter has been added.

Claim 30 has been amended to change "including" to "comprising" so as to mirror the format of the majority of the other claims. This amendment is clerical in nature and no new matter has been added.

Claim 31 has been amended to change "including" to "comprising" so as to mirror the format of the majority of the other claims and "the" has been added to make the claim more readable. "Nucleic acid" has been amended to read deoxyribonucleic acid, to mirror the language in Claim 1 and amended Claim 28. These amendments are clerical and/or linguistic in nature and no new matter has been added.

Claim 32 has been amended to specify that the system comprises a facility, connected to the computer network, *where* a plurality of bacterium samples from a plurality of patients or objects at a plurality of different locations *are obtained*, that the server receives the *nucleotide* sequence data, and to correct several linguistic and/or typographical issues. Support for these amendments may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines 15-16 and 21-23; Page 11, Lines 9-19; and Figures 1, 4A, and 4B. Accordingly, no new matter has been added.

Claim 33 has been amended to simplify the text of prior Claim 33. Support for these amendments may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines 15-16 and 19-23; Page 11, Lines 9-19; Page 13, Lines 7-10; Page 28, Lines 15-20; and Figures 1, 3, 4A, and 4B. Accordingly, no new matter has been added.

Claim 34 has been amended to specify that the plurality of bacterium samples are obtained at a *location physically separate* from where the *DNA* sequencing is performed. Support for these amendments may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines 15-16 and 21-23; Page 11, Lines 9-19; Page 17, Lines 3-6; Page 18, Line 13 to Page 19, Line 2; Page 24, Lines 6-8; and Figures 1, 4A, and 4B. Accordingly, no new matter has been added.

Claim 35 has been amended to specify that *the physically separate location* is a health care facility. Support for this amendment may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines 15-16 and 21-23; Page 11,

Lines 9-19; Page 17, Lines 3-6; Page 18, Line 13 to Page 19, Line 2; Page 24, Lines 6-8; and Figures 1, 4A, and 4B. Accordingly, no new matter has been added.

Claim 36 has been amended to specify that the sample is obtained at a *location physically separate* from where the *DNA* sequencing, comparing, and determination of a measure of phylogenetic relatedness *occurs*. Support for this amendment may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines 15-16 and 21-23; Page 11, Lines 9-19; Page 17, Lines 3-6; Page 18, Line 13 to Page 19, Line 2; Page 24, Lines 6-8; and Figures 1, 4A, and 4B. Accordingly, no new matter has been added.

Claim 38 has been amended to specify that *what may be an outbreak of bacterial infection is confirmed or refuted based upon the determination of phylogenetic relatedness*. Support for these amendments may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines 15-16 and 21-23; Page 11, Lines 9-19; Figures 1, 4A, and 4B; and former Claim 38. Accordingly, no new matter has been added.

Claim 44 has been amended to specify that, with regard to the system of Claim 32, *the DNA sequencing occurs at the facility and further wherein the nucleotide sequence data is transmitted over the computer network to the server*. Support for this amendment may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines 15-16 and 21-23; Page 11, Lines 9-19; Figures 1, 4A, and 4B; and former Claim 44. Accordingly, no new matter has been added.

Claim 45 has been added by the foregoing amendments. Claim 45 depends from Claim 32 and specifies that, with regard to the step of determining the phylogenetic relatedness between at least two compared samples, repeat sequences in the nucleotide sequence data from each sample are identified and the insertion or deletion of a repeat sequence is treated as a single genetic event. Support for this amendment may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines

15-16 and 21-23; Page 11, Lines 9-19; Page 24, Lines 19-21; Page 28, Line 15 to Page 36, Line 18; Figures 1, 3, 4A, 4B, 5, and 6; and Claim 32. Accordingly, no new matter has been added.

Claim 46 has been added by the foregoing amendments. Claim 46 depends from Claim 32 and specifies that, with regard to the step of determining the phylogenetic relatedness between at least two compared samples, individual single nucleotide polymorphisms in the nucleotide sequence data from each sample are identified and the insertion or deletion or change of an individual nucleotide is treated as a single genetic event. Support for this amendment may be found throughout the Specification, and at least at Page 8, Line 3 to Page 9, Line 6; Page 10, Lines 15-16 and 21-23; Page 11, Lines 9-19; Page 24, Lines 19-21; Page 28, Line 15 to Page 36, Line 18; Figures 1, 3, 4A, 4B, 5, and 6; and Claims 1, 16, 17, and 32. Accordingly, no new matter has been added.

Rejections Under 35 U.S.C. § 112, Second Paragraph – Indefiniteness

Former Claims 32, 33, 34-36, 38, and 44 were rejected under 35 U.S.C. § 112, Second Paragraph, as purportedly indefinite. *Final Official Action Purportedly Mailed February 5, 2007, Pages 2-3.* These rejections are respectfully traversed.

Not to acquiesce in the Examiner's rejections, but solely to facilitate prosecution, Applicants have, by the foregoing claim amendments, amended, *inter alia*, Claims 32, 33, 34-36, 38, and 44 to further clarify Applicants' invention. Applicants believe these amendments have rendered moot the Examiner's indefiniteness concerns and respectfully request withdrawal of the rejections of Claims 32, 33, 34-36, 38, and 44 under 35 U.S.C. § 112, Second Paragraph.

Rejections Under 35 U.S.C. § 103(a) – CDC 1998 Plan In View Of Frothingham

Claims 1, 3-5, 8, 10-14, 16, 17, 21-27, 32-36, 38, and 44 were rejected under 35 U.S.C. § 103(a) as purportedly obvious over "*Preventing Emerging Infectious Diseases: A Strategy for the 21st Century*," by the Centers for Disease Control and Prevention (October 1998) ("the CDC 1998 Plan") in view of R. Frothingham and W. A. Meeker-O'Connell, "*Genetic diversity in the* Mycobacterium tuberculosis *complex based on variable numbers of tandem DNA repeats*," 144 MICROBIOLOGY 1189-1196 (1998) ("Frothingham"). *Final Official Action Purportedly Mailed February 5, 2007, Pages 3-6.* According to the Examiner, "[i]t would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the VNTR sequencing of Frothingham in the CDC Plan for controlling and tracking infection." *Id. at Page 6.* This rejection is respectfully traversed.

When deciding whether obviousness exists, one needs to (A) determine the scope and contents of the prior art; (B) ascertain the differences between the prior art and the claims; (C) resolve the level of ordinary skill in the art; and (D) evaluate evidence of secondary considerations. *M.P.E.P. § 2141; Graham v. John Deere Co.*, 383 U.S. 1 (1966); *see also KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. ___ (Apr. 30, 2007). Moreover, "[i]f the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious." *In re Ratti*, 270 F.2d 810 (C.C.P.A. 1959); *M.P.E.P. § 2143.01.*

Applicants respectfully submit that the CDC 1998 Plan and Frothingham do not render Applicants' invention obvious at least because Frothingham uses image-based PCR methods to determine the lengths of PCR products which are then used to determine the number of repeats present. After the length-based PCR tests are conducted in Frothingham, certain PCR products are sequenced directly, but only to confirm that the PCR product

corresponded to the expected regions. Frothingham does not pertain to DNA sequencing, *per se*, much less Applicants' DNA sequencing to determine the relatedness of bacterium samples so as to track the spread of infectious bacteria.

Moreover, Frothingham relies upon a DNA size-based approach, whereas Applicants' invention relies upon a DNA *sequence*-based approach. If one were to apply the size-based approach of Frothingham to Applicants' invention, false positive results could be obtained because the sequences of a plurality of bacterium samples could have the same length, yet not the same actual nucleotide sequence. Frothingham is silent as to Applicants' method of doing actual *DNA sequencing* to differentiate strains.

Because Frothingham requires the operation of a principle different from Applicants' invention and because the CDC 1998 Plan lacks any substantive relation to Applicants' invention, Applicants respectfully request withdrawal of the 35 U.S.C. § 103(a) obviousness rejection of Claims 1, 3-5, 8, 10-14, 16, 17, 21-27, 32-36, 38, and 44 over the CDC 1998 Plan in view of Frothingham.

Rejections Under 35 U.S.C. § 103(a) – CDC 1998 Plan In View Of van Belkum

Claims 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, 38, and 44 were also rejected under 35 U.S.C. § 103(a) as allegedly obvious over the CDC 1998 Plan in view of A. van Belkum et al.'s, "Short-Sequence DNA Repeats in Prokaryotic Genomes," 62(2) MICROBIOLOGY AND MOLECULAR BIOLOGY REVIEWS 275-293 (June 1998) ("van Belkum"). *See Final Official Action Purportedly Mailed February 5, 2007, Pages 6-9.* According to the Examiner, "[i]t would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the repeat sequence region sequencing of [van] Belkum in the CDC Plan for controlling and tracking infection." *Id. at Page 9.* This rejection is respectfully traversed.

The considerations to be made when deciding obviousness are set forth above. Applicants respectfully submit that the CDC 1998 Plan in view of van Belkum do not render Applicants' invention obvious because van Belkum is a general review article that describes techniques which employ the same process as Frothingham, *i.e.*, generic, image-based typing that was common at the time. Like Frothingham, the techniques described in van Belkum do not pertain to DNA sequencing, *per se*, much less DNA sequencing to determine the relatedness of bacterium samples so as to track the spread of infectious bacteria.

Further like Frothingham, van Belkum reports techniques that utilize a DNA size-based approach, whereas Applicants' invention utilizes a DNA *sequence*-based approach. If one were to apply the size-based approaches described in van Belkum to Applicants' invention, false positive results could be obtained because the sequences of a plurality of bacterium samples could have the same length, yet not the same actual nucleotide sequence. van Belkum is silent as to Applicants' method of doing actual *DNA sequencing* to differentiate strains.

Moreover, and as noted during the Interview, even if one were to ignore the DNA-size versus DNA-sequence distinction between the cited publications and Applicants' invention, van Belkum actually teaches away from Applicants' invention by noting that: (1) there is "some debate on the clinical and epidemiological validity of" "PCR assays aiming at the amplification of the repeat locus in the staphylococcal protein A gene" (Page 284, left column, first full paragraph); and (2) SSRs in molecular epidemiology face "[a] major drawback . . . for studying epidemiology might be that regions under environmental pressure behave as hypervariable targets. This may restrict the general application of these regions for molecular typing of bacterial strains." (Page 287, right column, first full paragraph). With regard to (1), this statement in van Belkum cites reference 195, which is van Belkum *et al.*'s "*Are Variable Repeats in the* spa *Gene Suitable Targets for Epidemiological Studies of Methicillin-Resistant* Staphylococcus aureus *Strains?*," 15 EUR. J.

CLIN. MICROBIOL. INFECT. DIS. 768-69 (1996), attached (and formerly cited in Applicants' First Information Disclosure Statement and corresponding form PTO-1449, filed May 11, 2001). This paper states, "Even **without sequence analysis** of the individual units, it is obvious that the *spa* repeats may behave in a hypervariable, unstable manner that is unrelated to the overall evolution of the *Staphylococcus aureus* genome. **This implies that this marker probably should *not* be applied for the study of the epidemiological behaviour of this species.**" *Page 768, right column, end of first paragraph* (emphases added).

Because van Belkum reports on techniques that require the operation of a principle different from Applicants' invention and because the CDC 1998 Plan lacks any substantive relation to Applicants' invention, Applicants respectfully request withdrawal of the 35 U.S.C. § 103(a) obviousness rejection of Claims 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, 38, and 44 over the CDC 1998 Plan in view of van Belkum.

CONCLUSION

It is respectfully submitted that all rejections have been overcome by the above amendments and remarks. Thus, a Notice of Allowance is respectfully requested.

In the event that there are any questions relating to this Amendment and Reply After Final Rejection Pursuant To 37 C.F.R. § 1.116, or to the application in general, it would be appreciated if the Examiner would contact Applicants' undersigned attorney by telephone at (202) 373-6000 so that prosecution of the application may be expedited.

The Director is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Deposit Account No. 50-4047.

Respectfully submitted,
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